PHARMACOLOGICAL CHARACTERIZATION OF GASTROINTESTINAL BOMBESIN RECEPTOR SUBTYPES: IMPLICATIONS IN BOMBESIN SATIETY. Ellen Ladenhein, Dept. of Psychiatry and Behavioral Sciences, John Hopkins University School of Medicine, Baltimore, MD.

Bombesin (BN) and the related mammalian peptides gastrin-releasing peptide (GRP) and neuromedin B (NMB) suppress food intake after peripheral administration in rats. It has recently been demonstrated that there are two distinct subtypes of BN receptors, one with a high affinity for GRP (GRP-preferring) and the other with a high affinity for NMB (NMB-preferring). Since BN binds to both GRP and NMB-preferring receptors, it is not known which receptor subtype mediates the suppression of food intake by peripherally administered BN or where these receptors are localized. In order to address these questions we used a potent BN receptor antagonist [D-F_5-Phe^6, D-Ala^{11}]BN(6-13)methyl ester (ME) which has >5,000-fold selectivity for the GRP-preferring subtype over the NMB-preferring subtype. We examined the ability of ME to block the inhibition of food intake produced by BN, GRP 18-27 and NMB. Our results indicate that the suppression of food intake by peripherally administered BN-like peptides is mediated through the GRP-preferring receptor subtype. To determine potential sites where peripherally administered BN may act to inhibit feeding we examined the ability of ME and NMB to displace binding of ^{125}I-(Tyr^4)BN in the rat gastrointestinal tract. Our results demonstrate that although the gastrointestinal tract contains both GRP and NMB-preferring receptor subtypes, particularly high densities of GRP-preferring sites were found in the circular muscle layer of the stomach. These data are consistent with previous studies implicating a gastric site for BN's effects on food intake (Kirkham et al., 1991), however additional studies will be required to determine the importance of these receptors in the suppression of food intake by BN-like peptides.